# Natural History of Cholelithiasis in Patients with Alcoholic Cirrhosis (Cholelithiasis in Cirrhotic Patients)

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**To assess the natural history of cholelithiasis in patients with cirrhosis, 32 charts coded for both diseases were retrospectively reviewed. Cholecystectomy was performed in 22 patients. Only two patients met criteria for acute cholecystitis and two patients had suspected choledocholithiasis. Despite the high incidence of preoperative jaundice (32%), no common duct stones were documented. There was no operative mortality. The complication rate was 45%. In 10 patients not operated upon, two patients died of liver failure and the remaining eight patients are alive 8 months to 13 years after diagnosis (mean: 46 months) with no active biliary disease. It is concluded that: (1) jaundice in this subpopulation most often reflects hepatocellular injury and rarely biliary tract obstruction, (2) there appears to be a much lower incidence of acute cholecystitis and choledocholithiasis in cirrhotic patients with cholelithiasis than in the normal population, and (3) patients with cirrhosis and asymptomatic cholelithiasis can be safely managed without operation.**

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THE MANAGEMENT OF cholelithiasis in the patient with alcoholic cirrhosis is a frequent dilemma facing the general surgeon. The risks of operation must be weighed against the likelihood of cholelithiasis progressing to acute cholecystitis or common duct obstruction. The high morbidity and mortality of cholecystectomy in the patient with alcoholic cirrhosis has been well documented.[1-3] With this established surgical risk, knowledge of the natural history of cholelithiasis in this population becomes important. Two large autopsy series[4,5] suggest that the incidence of cholelithiasis in the patient with cirrhosis is twice that of the noncirrhotic population, and that the male to female ratio among cirrhotic patients with gallstones approaches 1:1 instead of the usual female predominance. Significantly, in these autopsy series, two thirds of the patients had bilirubinate stones in contrast to the usual incidence of only 15–20%. This finding is implicated by Nicholas et al. in explaining the rarity of cholecystitis and obstructive jaundice in cirrhosis.[4]

The purpose of this study was to investigate the clinical features of a group of patients with concomitant cirrhosis and cholelithiasis. An understanding of the natural history of this combination of diseases, as well as documentation of the risk of surgical intervention, is critical to the surgeon in planning the management of these patients.

## Methods

Of 1865 patients with cirrhosis, 32 had charts coded for both cirrhosis and cholelithiasis. These 32 patients formed the basis for this retrospective review. The method of diagnosis for both cirrhosis and cholelithiasis, indications for cholecystectomy, if performed, and associated signs and symptoms of cholelithiasis were recorded. Charts of patients who had cholecystectomy were reviewed for assessment of their intraoperative and postoperative courses. In an effort to identify factors predictive of significantly increased intraoperative bleeding, eight criteria were analyzed (using Students' unpaired t-test) for two groups: one with intraoperative blood loss less than 350 mL, and the other with blood loss greater than 350 mL. Finally, the stones of patients who had cholecystectomy were categorized according to the surgeons' and the pathologists' descriptions. Criteria used for classification were as follows: a stone was classified as the pigment variety only if it was black and as a cholesterol stone if it was white or yellow. All other stones were classified as mixed stones.

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TABLE 1. *Clinical Features of 22 Patients with Cirrhosis who had Cholecystectomy for Cholelithiasis*

| | No. of Patients | % |
|---|---|---|
| Preoperative assessment | | |
| Varices, esophageal | 10 | 45 |
| Hepatomegaly | 15 | 68 |
| Splenomegaly | 13 | 59 |
| Ascites | 14 | 67 |
| Jaundice | 7 | 32 |
| Indications for cholecystectomy | | |
| Biliary tract symptoms | 13 | 59 |
| Acute cholecystitis | 2 | 9 |
| Suspected choledocholithiasis | 2 | 9 |
| Asymptomatic | 4 | 18 |
| Other | 1 | 5 |
| Operative data | | |
| Choledocholithiasis | 0 | 0 |
| Morbidity | 10 | 45 |
| Mortality | 0 | 0 |

## Results

Of the 32 patients in this study, 29 had biopsy-proven cirrhosis. Three patients who did not have biopsy fulfilled the clinical criteria for a diagnosis of cirrhosis, having varices, encephalopathy, or ascites. The mean age of the group was 50 years at the time of diagnosis of cholelithiasis, with a range of 19–67 years. There were 14 females (44%) and 18 males (56%). Twenty-seven patients were white, two were black, and three were American Indian.

The diagnosis of cholelithiasis was made by ultrasonography in 28 patients, endoscopic retrograde cholangiopancreatography (ERCP) in two patients, oral cholecystography in one patient, and at surgical exploration in one patient. All charts were reviewed for signs and symptoms of cholelithiasis and cirrhosis, but in patients subsequently undergoing cholecystectomy, only signs and symptoms present before surgery were included. Hepatomegaly was present in 78% of patients, ascites in 59%, splenomegaly in 69%, jaundice in 69%, encephalopathy in 59%, varices in 47%, and acute pancreatitis in 25%. Twenty-two of the 32 patients had cholecystectomy (Table 1). The indications for cholecystectomy were abdominal pain, nausea, and vomiting in 18% of patients, pain without nausea and vomiting in 36%, nausea and vomiting alone in 5%, acute cholecystitis in 9%, (documented leukocytosis and fever in addition to symptoms), and suspected common duct stones in 9%. One patient had cholecystectomy during an exploratory laparotomy to rule out a liver mass, and four patients were asymptomatic (18%).

To evaluate the intraoperative course, patients were grouped according to four Childs' criteria: serum bilirubin, serum albumin, ascites, and neurologic condition. Among the 22 patients who had cholecystectomy, six (27%) were Class A, 14 (63%) were Class B, and two (10%) were Class C. The mean duration of surgery was 2 hours and 6 minutes. There was no statistically significant difference between Childs' Class A and Class B patients in this regard. The two patients in the Childs' Class C category had splenectomy and colectomy at the time of cholecystectomy and were therefore not suitable for comparison. The mean estimated blood loss for all patients was 362 mL. Although the patients in Childs' Class B had a greater mean blood loss (421 mL) compared with patients in Class A (mean: 252 mL), the difference was not significant (Student's unpaired t-test). Drains were placed at surgery in 21 of 22 patients and removed after an average of 2.2 days. A regular diet was resumed 4.7 days after operation, and patients were discharged an average of 8.8 hospital days after cholecystectomy.

All 22 patients who had cholecystectomy had an intraoperative cholangiogram. One finding on cholangiogram suggested a stone in the distal duct that was not confirmed at choledochotomy, the only such exploration performed. There were no operative deaths among the 22 patients.

The overall complication rate was 45%, including one wound infection, one episode of postoperative cholangitis (in the patient who had common duct exploration), and one persistent postoperative fever attributable to a urinary tract infection and/or atelectasis. The most frequent postoperative complication was leakage of ascitic fluid from the drain site after the drain had been removed. This occurred in five patients (23%), all of whom had ascites before operation. One patient required reoperation for closure of the drain site leak.

To evaluate factors predictive of the magnitude of intraoperative blood loss, the following parameters were compared between two groups based on estimated intraoperative blood loss (Group I $\geq$350 mL, Group II <350 mL): prothrombin time, serum albumin, bilirubin, alkaline phosphatase, and physical findings of encephalopathy, ascites, hepatomegaly, and splenomegaly. Only prolongation of prothrombin time and the presence of encephalopathy correlated significantly with intraoperative hemorrhage. In Group I, the prothrombin time was prolonged by 3.1 seconds compared with 0.28 second in Group II. Encephalopathy was diagnosed in 33% of the patients in Group I but in none in Group II.

Stone analyses were available in 15 of 22 patients who had cholecystectomy. Pigment stones were noted in 67%, cholesterol stones in 6%, and mixed stones in 27%. Multiple stones were present in 85% of the group.

## Discussion

The group of patients with both cirrhosis and cholelithiasis, although similar to noncirrhotic patients with

cholelithiasis with respect to age, were dissimilar with regard to other factors. Our series, as well as the autopsy series of Nicholas et al. and Bouchier,[4,5] suggest a comparable occurrence of cholelithiasis in male and female patients with cirrhosis, whereas in the noncirrhotic population, a 3:1 female predominance is reported.[6–10] Although our study was not designed to address the issue of the incidence of stones among patients with cirrhosis, others have reported a 30% incidence, twice that in the noncirrhotic population.[4,5] These observations suggest that cirrhosis may augment the development of cholelithiasis. Although bacteremia in this group of patients seemed rare, there was a 60–80% incidence of ascites, organomegaly, encephalopathy, and jaundice.

Of particular interest is the significance of hyperbilirubinemia in the patients who had cholecystectomy. Seven of 22 patients had jaundice before operation (32%). In patients with normal liver function, jaundice clearly predicts a high likelihood of contemporaneous choledocholithiasis, the reported incidence ranging from 59–81%.[6–8,10] However, in our series of patients with cirrhosis, as well as that reported by Aranha et al.,[1] jaundice was far more common yet no common duct stones were found.

This experience suggests that even in jaundiced cirrhotic patients with right upper quadrant pain, a normal ultrasonographic examination suggests hepatocellular decompensation; the patient should be observed. However, if either gallstones or ductal dilatation is demonstrated by ultrasonography, it would seem prudent to proceed with ERCP in order to rule out choledocholithiasis.

Only two patients in our series met the criteria for acute cholecystitis. The infrequency of acute cholecystitis as an indication for cholecystectomy is in striking contrast to that seen in the noncirrhotic population, in which acute cholecystitis is the indication for cholecystectomy in 18–20% of patients.[8,11,12] Schwartz[2] and Castaing et al.[3] have likewise noted the much lower incidence (10% and 6%, respectively) of acute cholecystitis as an indication for cholecystectomy in patients with cirrhosis. The much lower incidence of both acute cholecystitis and common duct obstruction in cirrhotic patients with cholelithiasis may relate to the higher incidence of bilirubin stones. The smaller size and greater friability of pigment stones make them less likely to obstruct either the cystic or the common ducts. They are more likely to fragment and pass through the ampulla without serious sequelae. A second important factor may be the more frequent discovery of truly asymptomatic cholelithiasis during investigation of jaundice triggered by episodes of hepatic decompensation.

There was no operative mortality among patients who had cholecystectomy in this series. Doberneck et al., however, noted a 35% mortality rate associated with alimentary and intraperitoneal operative procedures in patients with cirrhosis.[13] Schwartz reported no deaths during cholecystectomy among 11 patients with cirrhosis who had cholecystectomy and had normal liver function and coagulation studies, yet there was a 17% mortality rate in higher-risk cirrhotics who had cholecystectomy.[2] Similarly, Aranha et al. reported a 10% mortality rate after cholecystectomy in 43 cirrhotic patients with a prothrombin time prolonged less than 2.5 seconds, yet an 83% mortality rate when the prothrombin time was prolonged more than 2.5 seconds.[1]

The high mortality rate from surgical intervention in these patients is almost exclusively related to intraoperative bleeding. In addition to the coagulation abnormalities, Schwartz suggested that the hypervascular scar tissue resulting from the cirrhotic process itself promotes bleeding. In cases of anticipated severe bleeding or when extensive hemorrhage is encountered during operation, the use of vasopressin as a mesenteric vasoconstrictive agent may prove helpful.[2] Schwartz also successfully treated a patient with epsilon-aminocaproic acid when excessive fibrinolysis was encountered.[2]

Additional operative complications occurred in 41% of the group. The most common was ascitic leak from the site of drain removal. This resulted in significant morbidity, including rehospitalization in one patient and operative fascial closure in another. Perhaps because of the fear of bleeding complications, drains are usually placed (18 of 19 patients in our series). However, if ascites were present before operation, one third of the patients (36%) had a postoperative drain site leak. It would seem that meticulous intraoperative hemostasis combined with a selective, not routine, use of drains might decrease the incidence of this problem. Similarly, we believe that when drainage is indeed indicated, closed suction drains, not Penrose drains, should be chosen.

The gallstones of patients who had cholecystectomy in this group were most often bilirubinate (67%). Similarly, Bouchier found a 66% incidence of bilirubin stones in his autopsy series of 69 patients with both cirrhosis and cholelithiasis.[5] In contrast, among 517 patients without cirrhosis at autopsy, only 13% of gallstones were pigmented. Possible explanations include a decreased bile acid pool in cirrhosis[14] or an increase in the concentration of unconjugated bilirubin in the bile because of defective conjugation.[15] Perhaps a more likely explanation, however, is that the bilirubinate gallstones are precipitated by chronic hemolysis caused by ongoing hepatic necrosis and hypersplenism.[16–18]

Perhaps the most useful information in assessing the natural history of cholelithiasis and cirrhosis comes from those patients followed without surgical intervention. Two of 10 such patients in our series died of hepatic failure but without evidence of biliary obstruction. The remaining eight patients continue to do well 8 months to 13 years after the diagnosis of cholelithiasis was made. The latter

group shows no evidence of biliary obstruction nor biliary symptoms. We therefore recommend that patients with cirrhosis and asymptomatic cholelithiasis be followed without operation, thus avoiding the risk of surgery. However, if jaundice develops in a patient with cirrhosis, the presence or absence of common duct dilatation is assessed by ultrasonography. If the common duct is visualized yet not dilated, we observe the patient, since jaundice in this context nearly always represents hepatocellular decompensation. If cholelithiasis or a dilated common duct is visualized by ultrasonography, or if the common duct cannot be seen, then the patient should undergo ERCP. If choledocholithiasis is documented, then endoscopic sphincterotomy or a common duct exploration is performed, depending on the severity of the patient's cirrhosis. If, by ERCP, stones are seen only within the gallbladder, we would suggest conservative management since the risk of subsequent acute cholecystitis or common duct obstruction is remarkably low.

## Conclusion

Since the incidence of acute cholecystitis and choledocholithiasis in patients with cirrhosis occurs with approximately half the frequency as in noncirrhotic patients with cholelithiasis, jaundice in this context usually represents hepatocellular decompensation, seldom indicating biliary obstruction. When required, however, cholecystectomy can be performed in cirrhotic patients with low mortality, but morbidity is nonetheless appreciable. An algorithm for the investigation of the cirrhotic patient suspected of having cholelithiasis is presented.

Mechanical drains should be used sparingly after cholecystectomy in patients with cirrhosis since ascitic leakage from the drain site is common.

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